SUMMARY OF EXAMINER INTERVIEW

Applicants would like to thank Examiner Lisa Cook and Supervisory Patent Examiner Long Le for conducting an interview on for this case on February 28, 2008. Applicants submit this Summary setting forth a statement of the substance of the in-person interview that occurred on February 28, 2008.

Brief Description of the Nature of any Exhibit Shown or any Demonstration Conducted:

None.

Identification of the Claims Discussed:

Independent claims 1, 3 and 6.

Identification of Specific References Discussed:

U.S. Patent No. 6,358,939 to Hayes et al.

U.S. Patent No. 5,552,292 to Uchida et al.

Sreekant Murthy (Inflammation Research Association)

Sugi et al (The American Journal of Gastroenterology)

Identification of the Principle Proposed Amendments of a Substantive Nature Discussed:

None.

The General Thrust of the Principal Arguments of Applicant and the Examiner:

That the proposed claim limitations patentably distinguish over the aforementioned references and other prior art of record. None of the cited references teach comparing the lactoferrin level of a first human fecal sample from person with the lactoferrin level of a second human fecal sample taken from the same person at a later time to determine whether the person had an increase or decrease in gastrointestinal inflammation and to monitor IBD activity of the person.

REMARKS

Applicants respectfully request reconsideration of the present Application. Claims 1 and 6 have been amended herein. Claims 3-5 have been cancelled.

Rejections based on 35 U.S.C. § 112

Claims 1, 2 and 6 stand rejected under 35 U.S.C. §112, second paragraph as being indefinite. Applicants have amended the preamble as suggested. As such, Applicants request withdrawal of the §112 rejection of claims 1, 2 and 6.

Rejections based on 35 U.S.C. § 103

Claim 1-2 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Hayes et al. (US Patent No. 6,358,939 B1) in view of Sreekant Murthy, PhD (Inflammation Research Association, Newsletter, September & December 1999, Vol. 9, No. 3 & 4, pages 1-14 and in further view of Uchida et al. (US Patent No. 5,552,292). "). As the Hayes reference in view of the Sreekant Murthy reference and in further view of the Uchida reference fail teach or suggest all the limitations of the rejected claims, Applicants respectfully traverse this rejection, as hereinafter set forth.

Independent claim 1, as amended, is directed to method for monitoring a person having inflammatory bowel disease for gastrointestinal inflammation. A first human fecal sample from a person is obtained and the concentration of lactoferrin the first human fecal sample is determined. The first fecal sample is diluted. The first sample is contacted with immobilized polyclonal antibodies to endogenous lactoferrin to create a first treated sample. The first treated sample is contacted with enzyme-linked polyclonal antibodies to create a first readable sample. The optical density of said first readable sample is determined at 450nm. A purified lactoferrin standard curve is generated and a linear portion of the standard curve is

determined. The optical density of said first readable sample is compared to said standard curve to determine a concentration of the first diluted sample and to determine whether the concentration of the first diluted sample is within the linear portion of the standard curve. If the first diluted sample is within the linear portion of the standard curve, the concentration of total endogenous lactoferrin in said first fecal sample is determined.

A second human fecal sample from the same person is obtained at a time after the first sample was obtained and the concentration of lactoferrin in the second human fecal sample is determined. The lactoferrin concentration of the first fecal sample is compared to the lactoferrin concentration of the second sample for the person to monitor the inflammatory bowel disease activity of the person and determine if the person has had a decrease or increase in gastrointestinal inflammation.

Applicants submit that the Hayes reference fails to teach or suggest comparing the lactoferrin concentration of a first sample with the lactoferrin concentration of a second sample from the same human to determine if the person has had a decrease or increase in gastrointestinal inflammation. The invention of claim 1 is directed to a method that is sensitive enough to monitor changes lactoferrin levels at different times in the same human to determine if the person has had a change in gastrointestinal inflammation. This allows a physician to know whether an IBD flare may be imminent before the onset of symptoms or may allow a physician to know whether a treatment, such as a pharmaceutical, has been effective in decreasing gastrointestinal inflammation using a non-invasive method.

The Office Action points to Column 23, Lines 46-60 of the Hayes reference as teaching this limitation. However, upon inspection, Column 23, Lines 46-60 of the Hayes reference describes looking at symptoms of IBD, and not lactoferrin concentration, to determine

if a calcitriol treated mouse exhibited reduced symptoms of disease as compared to controls. Thus, while the Hayes reference describes that weight, fecal and blood hemoglobin and fecal lactoferrin of MICE are plotted as a function of time, no comparison is done and only symptoms of IBD are looked to determine if mice exhibit reduced symptoms of disease. Symptoms of IBD in the Hayes Reference are defined as "abdominal pain, diarrhea, rectal bleeding, weight loss, fever, loss of appetite, and other more serious complications, such as dehydration, anemia and malnutrition." *See* Column 3, Lines 15-25. Nowhere in the Hayes reference are symptoms defined as lactoferrin concentrations. Furthermore, the Hayes references fails to teach or suggest comparing the lactoferrin concentration of a first sample with the lactoferrin concentration of a second sample from the same human to determine if the person has had a decrease or increase in gastrointestinal inflammation. Rather, the Hayes reference makes no comparison of lactoferrin results taken at different times of the same individual (mouse). Likewise, Sreekant Murthy and Uchida fail to teach to teach or suggest comparing the lactoferrin concentration of a first sample with the lactoferrin concentration of a second sample from the same human to determine if the person has had a decrease or increase in gastrointestinal inflammation.

Furthermore, it would not be obvious to compare the lactoferrin concentration of a first sample with the lactoferrin concentration of a second sample from the same human to determine if the person has had a decrease or increase in gastrointestinal inflammation in view of the Hayes reference in view of the Sreekant Murthy reference in further the Uchida reference. The invention of claim 1 is directed to performing a diagnostic test for human IBD. There is a vast difference between human IBD and dextran sulfate induced ulcerative colitis. First, Sreekant Murthy reference describes a dextran sulfate model "resembles" chronic human ulcerative colitis and human colitis-associated colon cancer and can be used in preclinical trials

for pharmacological agents. Thus, while the dextran sulfate mouse model may be used for drug discovery, this does not mean it is sensitive enough to be used in diagnostics, especially human diagnostics.

The dextran sulfate model in a mouse is not an adequate model to be used in diagnostics for a variety of reasons. First, according to the Sreekant Murthy reference, the dextran sulfate mouse model "resembles" chronic human ulcerative colitis which is limited to the large bowel. The invention of claim 1, is directed to both types of IBD, ulcerative colitis and Crohn's disease. Crohn's disease in humans affects both the small and large bowel. Thus, a dextran sulfate mouse model that only affects the large bowel of a mouse is not sensitive enough to be used for a diagnostic for a human disease that affects both the small and large bowel. Second, Sreekant Murthy actually teaches away from use of the dextran sulfate mouse model in human diagnostics as the "it is difficult to produce an ideal model of IBD" and "investigators must be careful in interpreting the results" of the model. Clearly, based on the limitations of the dextran sulfate induced mouse model, the mouse model described in Sreekant Murthy is not sensitive enough for use in human diagnostics as the mouse model does not even cover the same portions of the digestive tract and there are vast differences anatomically between mice and humans.

Furthermore, it would not be obvious to compare the lactoferrin concentration of a first sample with the lactoferrin concentration of a second sample from the same human to determine if the person has had a decrease or increase in gastrointestinal inflammation in view of the Hayes reference in view of the Sreekant Murthy reference in further the Uchida reference due to the differences between human and mouse feces. Human feces over time varies in consistency and makeup depending on a person's diet and health. It would not have been obvious in view of

the combination of references to test the same human for a marker at different times and expect that the concentrations of lactoferrin would allow a determination of a decrease or increase in gastrointestinal inflammation.

First, the Hayes reference does not even teach comparing levels of lactoferrin taken from the same human (or even mouse for that matter) at different times to determine if there has been an increase or decrease in gastrointestinal inflammation, and second, it would not be obvious to do so as the Hayes reference dealt with mouse feces. Laboratory mouse feces varies greatly from human feces as a laboratory mouse has a consistent diet and other parameters that are controlled by researchers. Unlike mouse feces, human feces can vary greatly in consistency and make-up based human diet, health and lifestyle. To further support this contention, the reference O'Mahony et al (a copy of which is attached hereto), found fluctuations in fecal antibody levels depend on the consistency of the feces before sample (e.g., whether the feces were initially semi-liquid or liquid form) which confounds attempts to distinguish between disease states even after normalizing sample dilution. Thus, based on the prior art it would not have been obvious to compare lactoferrin concentrations for a human person taken at different times to determine if the person has had a decrease or increase in gastrointestinal inflammation due to the fluctuations in consistency and makeup of human feces.

Furthermore, serum and urine are typically utilized for monitoring the progress of human diseases. Serum and urine have less inherent test variation than that of human feces, and thus it would not be obvious that one could utilize fecal samples taken from the same human at different times to monitor the progression of a disease. As all the elements of independent claim 1 are not taught or suggested by the combination of references, Applicants request withdrawal of

the §103(a) rejection of claim 1. As claim 2 depends from claim 1, Applicants request withdrawal of the §103(a) rejection of this claim as well.

Claim 1, 2 and 6 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Hayes et al. (US Patent No. 6,358,939 B1) in view of Sreekant Murthy, PhD (Inflammation Research Association, Newsletter, September & December 1999, Vol. 9, No. 3 & 4, pages 1-14 and in further view of Sugi et al. (The American Journal of Gastroenterology, Vol. 91, No. 5, 927-934, 1996). As the Hayes reference in view of the Sreekant Murthy reference and in further view of the Sugi reference fail teach or suggest all the limitations of the rejected claims, Applicants respectfully traverse this rejection, as hereinafter set forth.

Claim 6 is directed to a method for monitoring a human having inflammatory bowel disease for gastrointestinal inflammation. The method comprises comparing the lactoferrin concentration from a first sample obtained from a human having inflammatory bowel disease to a second sample obtained from the same person at a second time after treatment of the human's IBD later than the first time to determine if the treatment has been effective in decreasing or eliminating gastrointestinal inflammation.

As discussed above, the Hayes reference and the Sreekant Murthy reference fails to teach or suggest comparing the lactoferrin concentration of a first sample with the lactoferrin concentration of a second sample from the same human to determine if the person has had a decrease in gastrointestinal inflammation.

Likewise, as stated in the Office Action, the Sugi reference "does not teach multiple sample collections at different times." *See* Office Action dated 1/16/2008, Page 9. Thus, the Sugi reference does not teach comparing the lactoferrin concentration of a first sample with the lactoferrin concentration of a second sample from the same human to determine if the

person has had a decrease in gastrointestinal inflammation. Furthermore, for the same reasons stated above, it would not be obvious to compare the lactoferrin concentration of a first sample with the lactoferrin concentration of a second sample from the same human to determine if the person has had a decrease in gastrointestinal inflammation in light of the combination of references.

As such, it is submitted that the Hayes reference in view of the Sreekant Murthy reference in further view of the Sugi reference fails teach or suggest all the limitations of the rejected claims, Accordingly, independent claims 1 and 6 are+ not anticipated by the Hayes reference in view of the Uchida reference and withdrawal of the 35 U.S.C. §103(a) rejection of this claim is requested. As claim 2 depends directly from claim 1, applicants request withdrawal of the §103(a) rejection of this claim as well.

CONCLUSION

For at least the reasons stated above, claims 1-2 and 6 are now in condition for allowance. Applicants respectfully request withdrawal of the pending rejections and allowance of the claims. If any issues remain that would prevent issuance of this application, the Examiner is urged to contact the undersigned – 816-474-6550 or jdickman@shb.com (such communication via email is herein expressly granted) – to resolve the same. It is believed that no fee is due, however, the Commissioner is hereby authorized to charge any amount required to Deposit Account No. 19-2112.

Respectfully submitted,

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